JUL 2 3 2012

510k Summary

Dimension® Alkaline Phosphatase Flex® reagent cartridge (ALPI)
Dimension® Alkaline Phosphatase Calibrator (ALPI CAL)

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

A. 510(k) Number - k121907

B. Applicant: Rose T. Marinelli
Siemens Healthcare Diagnostics, Inc.
P.O. Box 6101, Newark, DE 19714-6101
Office Number: 302-631-8805; Fax Number: 302-631-6299

C. Date: June 28, 2012

D. Proprietary and Established Names:

Dimension® Alkaline Phosphatase Flex® reagent cartridge, (ALPI)
Dimension® Alkaline Phosphatase Calibrator (ALPI CAL)

E. Regulatory Information:

Alkaline Phosphatase (ALPI) Flex® reagent cartridge

Regulation section: 21 CFR 862.1050 Alkaline phosphatase or isoenzymes test system
Classification: Class II
Product Code: CJO
Panel: Clinical Chemistry

Alkaline Phosphatase Calibrator (ALPI CAL)

Regulation section: 21 CFR 862.1150 Calibrator, Secondary
Classification: Class II
Product Code: JIT
Panel: Clinical Chemistry

F. Predicate Devices:

The predicate device used to demonstrate substantial equivalence to the Dimension® Alkaline Phosphatase (ALPI) Flex® reagent cartridge is the ADVIA® Chemistry Alkaline Phosphatase AMP Method previously cleared under k991576.

The predicate device used to demonstrate substantial equivalence to the Dimension® Alkaline Phosphatase Calibrator (ALPI CAL) is the Dimension Vista® Alkaline Phosphatase Calibrator previously cleared under k061818.

G. Device Description:

The ALPI method employs alkaline phosphatase that catalyzes the transphosphorylation of p-nitrophenylphosphate (p-NPP) to p-nitrophenol (p-NP) in the presence of the transphosphorylating buffer, 2 amino-2-methyl-1-propanol (AMP). The reaction is enhanced through the use of magnesium and zinc ions. The change in absorbance at 405 nm due to the formation of p-NP is directly proportional to the ALP activity, since other reactants are present in non-rate limiting quantities and is measured using a bichromatic (405, 510 nm) rate technique.

$$\text{p-NPP} + \text{AMP} \xrightarrow[\text{pH 10.25}\ \text{Mg/Zn}]{\text{ALP}} \text{p-NP} + \text{AMP} + PO_4$$

The ALPI CAL is a three (3) level, liquid calibrator. It is packaged as a kit of six vials, two vials per level (1, 2 and 3) with 1.0 mL per vial. The product matrix is a human serum albumin based product containing alkaline phosphatase from porcine kidney. Level 1 is zero. Levels 2 and 3 contain alkaline phosphatase at the following concentrations.

Level	Alkaline Phosphatase U/L
1	0
2	500
3	1000

This product is sold separately from the Flex® reagent cartridge. Values are assigned to new lots from a Masterpool that is from an International Federation of Clinical Chemistry (IFCC) reference.

H. Intended Use:

The ALPI method is an *in vitro* diagnostic test for the quantitative measurement of alkaline phosphatase in human serum and plasma on the Dimension® clinical chemistry system. Measurements of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid, and intestinal diseases.

ALPI CAL is an *in vitro* diagnostic product for the calibration of alkaline phosphatase (ALPI) method on the Dimension® clinical chemistry system.

I. Indication(s) for Use:
Same as Intended Use

J. Substantial Equivalence Information:

Both the Dimension® Alkaline Phosphatase Flex® reagent cartridge (ALPI) assay and the predicate ADVIA® Chemistry Alkaline Phosphatase AMP assay employ prepackaged reagents for use on an automated clinical chemistry test systems. A comparison of the similarities and differences between the devices is provided in the following tables:

Similarities for Dimension® ALPI assay:

Feature	Dimension® Alkaline Phosphatase Flex® reagent cartridge (DF150)	Predicate: ADVIA® Chemistry Alkaline Phosphatase AMP k991576
Intended Use	The ALPI method is an *in vitro* diagnostic test for the quantitative measurement of alkaline phosphatase in human serum and plasma on the Dimension® clinical chemistry system. Measurements of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid, and intestinal diseases.	For *in vitro* diagnostic use in the quantitative determination of alkaline phosphatase in human serum and plasma on the ADVIA® Chemistry systems. Such measurements are used in the diagnosis and treatment of hepatobiliary and bone disease.
Sample Type	Serum and Lithium Heparin Plasma	Serum and Lithium Heparin Plasma
Measurement	Bichromatic rate	Rate (RRA)

Differences for Dimension® ALPI assay:

Feature	Dimension® Alkaline Phosphatase Flex® reagent cartridge (DF150)	Predicate: ADVIA® CHEMISTRY® Alkaline Phosphatase AMP Method k991576
Measuring Range	10 - 1000 U/L	0 - 1100 U/L
Sample Size	7 µL	3 µL

Similarities for Dimension® ALPI Calibrator

Feature	Dimension® Alkaline Phosphatase Calibrator ALPI CAL (DC150)	Predicate: Dimension Vista® Alkaline Phosphatase Calibrator ALP CAL (KC330) k061818
Intended Use	ALPI CAL is an *in vitro* diagnostic product for the calibration of alkaline phosphatase (ALPI) method on the Dimension® clinical chemistry system.	The ALP CAL is an *in vitro* diagnostic product for the calibration of Alkaline Phosphatase (ALP) method on the Dimension Vista® System.
Preparation	Liquid: Provided ready to use.	Liquid: Provided ready to use.
Storage	2 – 8 °C	2 – 8 °C

Differences for Dimension® ALPI CAL

Feature	Dimension® Alkaline Phosphatase Calibrator ALPI CAL (DC150)	Predicate: Dimension Vista® Alkaline Phosphatase Calibrator ALP CAL (K330) k061818
Matrix	Human serum albumin based	Bovine protein based
Target Concentrations	Level 1: 0 U/L Level 2: 500 U/L Level 3: 1000 U/L	Level 2: (CAL A) 1040 U/L Note: Level 1 is System Water
Traceability	IFCC reference method	Masterpool values

K. Standard/Guidance Document Reference:

- Evaluation of Precision Performance of Quantitative Measurement in Methods; Approved Guideline (EP5-A2)
- Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline (EP6-A)
- Interference Testing in Clinical Chemistry; Approved Guideline (EP7-A2)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP9-A2)
- Protocols for Determination of Limits of Detection and Quantitation; Approved Guideline (EP17-A)
- Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline (C28-A3)

L. Performance Characteristics

The following data represent typical performance for the Dimension® clinical chemistry systems and was collected on a Dimension® RxL.

Method Comparison

Split sample comparison between the Dimension® Alkaline Phosphatase assay and the ADVIA® Chemistry Alkaline Phosphatase AMP assay gave the following correlation statistics, when tested with patient samples:

Dimension® Alkaline Phosphatase (ALPI) vs. Predicate

Dimension®	Predicate	Slope	Intercept U/L	Correlation Coefficient (r)	n
ALPI	ADVIA® ALPAMP	1.06	-0.4	0.999	116

Serum/Plasma Comparison

To demonstrate equivalency between serum and lithium heparin plasma for DM ALPI, comparison testing of 50 matched serum and lithium heparin plasma samples were tested on the Dimension® clinical chemistry system and gave the following linear regression statistics:

Serum vs. Plasma Comparison Data

Serum vs.	Slope	Intercept U/L	Correlation Coefficient (r)	n
Lithium Heparin Plasma	1.02	-5.08	0.999	50

Reference Interval (Expected Values)

Samples were collected from 132 healthy adults and analyzed with the Dimension® ALPI method. The reference interval was calculated non-parametrically and represents the central 95% of results determined from the population.
Expected Values: 46-116 U/L [0.77 – 1.94 µkat/L]

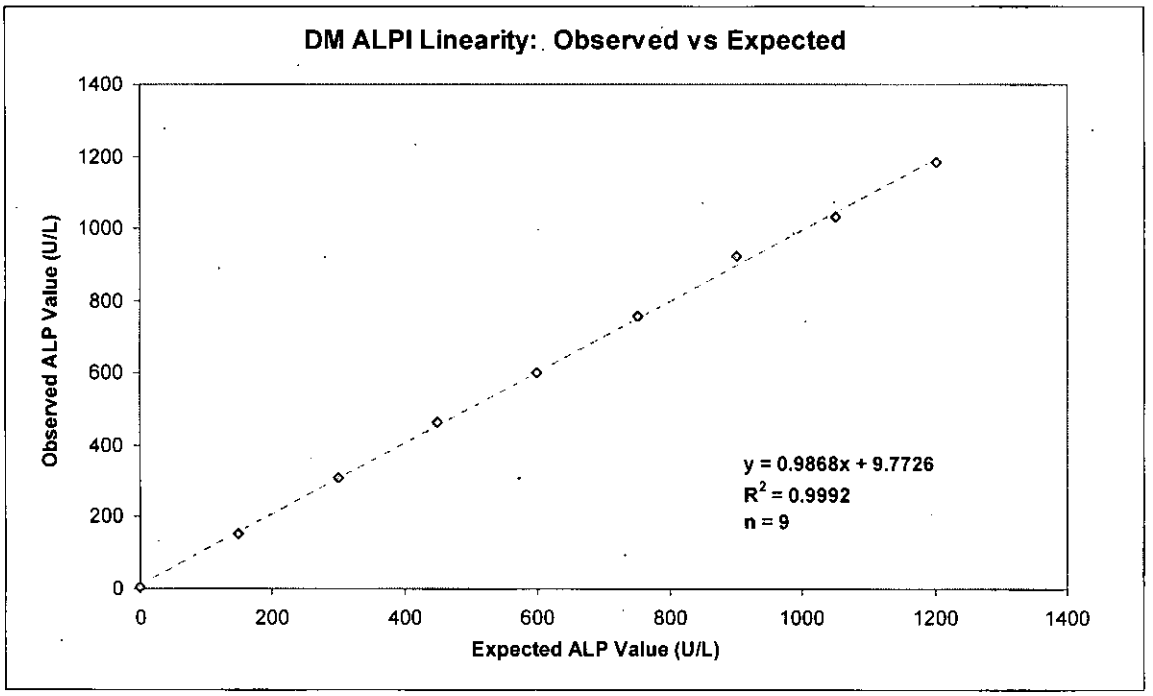
Precision

Precision testing was performed in accordance with CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition. Samples consisted of three levels of Bio-Rad® Multiqual Assayed Quality Controls and two serum pools. Testing was performed over 20 days, two separate runs with two test samples for each test material. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP5-A2. The data are summarized in the following table:

		Repeatability		Within-Lab	
Sample n=80	Mean (U/L)	SD (U/L)	%CV	SD (U/L)	%CV
BioRad® Multiqual Assayed QC					
Level 1	37	0.6	1.5	1.6	4.2
Level 2	157	1.0	0.6	3.7	2.3
Level 3	303	3.3	1.1	7.1	2.4
Pools					
Serum Pool 1	81	1.1	1.4	1.8	2.2
Serum Pool 2	842	5.7	0.7	13.3	1.6

Linearity

The linear range was determined according to CLSI EP-6A, *Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline.* Based on the results of this testing and the Limit of Detection testing on the Dimension® clinical chemistry analyzer, the analytical measurement range was determined to be 10 – 1000 U/L.



Analytical Specificity/Interferences

The ALPI method was evaluated for interference according to CLSI EP7-A2 Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference.

Substance Tested	**Substance Concentration**	**Alkaline Phosphatase** U/L [µkat/L]	%	**Bias**
Hemoglobin (hemolysate)	1000 mg/dL [0.62 mmol/L]	297[4.96]		<10
		823 [13.74]		<10
Bilirubin (unconjugated)	80 mg/dL [1026 µmol/L]	300 [5.01]		<10
		834 [13.92]		<10
Bilirubin (conjugated)	80 mg/dL [1026 µmol/L]	307 [5.12]		<10
		856 [14.29]		<10
Lipemia (Intralipid®)	500 mg/dL [5 g/L]	308 [5.14]		<10
		878 [14.66]		<10
	600 mg/dL[6 g/L]	308 [5.14]		**
		878 [14.66]		**

**Lipemia ((Intralipid®) at 600 mg/dL and above tripped an error flag on this method; interference could not be determined.

Studies were also performed following CLSI EP7-A2 for Interference Testing of exogenous substances at an alkaline phosphatase concentration of 299 U/L and 842 U/L and were found not to interfere with the ALPI method when present in serum and plasma. Inaccuracies (biases) were all less than 10%. See Instructions for Use for a full list of substances tested.

Limit of Blank, Limit of Determination and Limit of Quantitation

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) was evaluated in accordance with CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline. Studies were performed on the Dimension® clinical chemistry analyzer with the following results:

Dimension® Alkaline Phosphatase (ALPI)		
Limit	**Protocol**	**Value**
LoB	5 samples of Enzyme Diluent (zero level) were tested for 3 days, one run per day, 2 replicates per run, 2 reagent lots, 1 instrument	3 U/L
LoD	5 low level samples were tested for 3 days, one run per day, 2 replicates per run, 2 reagent lots, 1 instrument	8U/L
LoQ	3 low level samples diluted with enzyme diluent were tested for 3 days, one run per day, 3 replicates per run, 2 reagent lots, 1 instrument	9 U/L

Calibrator

For opened products, once the cap is removed, assigned values are stable for 30 days when recapped immediately after use and stored at 2-8°C.

For unopened product, see the expiration date on the calibrator carton.

M. Conclusion: The Dimension® Alkaline Phosphatase (ALPI) Flex® reagent cartridge with the associated Dimension® Alkaline Phosphatase Calibrator (ALPI CAL) are substantially equivalent in principle and performance to the ADVIA® Chemistry Alkaline Phosphatase AMP assay and Dimension Vista® Alkaline Phosphatase (ALP) calibrator respectively.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Siemens Healthcare Diagnostics
c/o Rose T. Marinelli
P.O. Box 6101
Newark, DE 19701

JUL 23 2012

Re: k121907
Trade Name: Dimension® Alkaline Phosphatase (ALPI) Flex® reagent cartridge
Dimension® Alkaline Phosphatase Calibrator (ALPI CAL)
Regulation Number: 21 CFR §862.1050
Regulation Name: Alkaline phosphatase or isoenzymes test system
Regulatory Class: Class II
Product Codes: CJO, JIT
Dated: June 28, 2012
Received: June 29, 2012

Dear Ms Marinelli:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance...

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use Form

510(k) Number (if known): k121907

Device Name: **Dimension® Alkaline Phosphatase Flex® reagent cartridge (ALPI)**

Indications for Use:

The ALPI method is an *in vitro* diagnostic test for the quantitative measurement of alkaline phosphatase in human serum and plasma on the Dimension® clinical chemistry system. Measurements of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid, and intestinal diseases.

Prescription Use ____X___ (Part 21 CFR 801 Subpart D)	AND/OR	Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device

Evaluation and Safety

510(k) K121907

Indications for Use Form

510(k) Number (if known): k121907

Device Name: **Dimension® Alkaline Phosphatase Calibrator (ALPI CAL)**

Indications for Use:

ALPI CAL is an *in vitro* diagnostic product for the calibration of alkaline phosphatase (ALPI) method on the Dimension® clinical chemistry system.

Prescription Use ____X___ (Part 21 CFR 801 Subpart D)	AND/OR	Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device

Evaluation and Safety

510(k) k121907